c.) Remarks

Claim 1 has been amended in order to recite the present invention with the specificity required by statute. Additionally, claims 19 and 20 are amended for better dependent format. The subject matter of the plainly ministerial amendment is found from page 12, line 15 to page 22, line 11, and at page 36, lines 22-25. Accordingly, no new matter is added, as will be explained below in detail.

At the time the present application was filed, the process for producing a sugar nucleotide utilized a) a microorganism capable of producing NTP from a nucleotide precursor,[1/] and b) a culture broth of a microorganism capable of producing a sugar nucleotide from a sugar and NTP[2] were used as enzyme sources. However, in the previous amendment, due to word processing error, "a sugar and NTP" was inadvertently changed to --a sugar--. This has been corrected above.

The amendment filed September 25, 2002 is objected to under 35 U.S.C. §132. The Examiner states that the support for specific use of a culture broth of a microorganism capable of producing GTP or UTP from a nucleotide precursor as an enzyme has not been found. To the extent such is maintained, this rejection is respectfully traversed.

Respectfully submitted, this rejection is without basis in fact at least for the following reasons. It is common knowledge in the art that NTP (nucleotide-5'-triphosphate) is a general term of GTP (guanosine-5'-triphosphate), UTP (uridine-5'-triphosphate), CTP (cytidine-5'-triphosphate) and TTP (thymidine-5'-triphosphate).

As shown at page 12, lines 4-14, the specification discloses "a microorganism capable of producing NTP from a nucleotide", and exemplifies microorganisms belonging

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1/ Or a treated product of the culture broth.

to the genii *Corynebacterium* and *Escherichia.* As discussed above, since GTP and UTP are taught by "NTP", the description at page 14, lines 4-14 teaches "a microorganism capable of producing GTP or UTP from a nucleotide".[3/]

The enzyme source b) used in the process for producing a sugar nucleotide in claim 1 is "a culture broth or culture broths of at least one strain of a microorganism having genes responsible for production of guanosine diphospho-sugar ("GDP-sugar") or uridine diphospho-sugar("UDP-sugar") from a sugar ... and GTP or UTP". This is explicitly shown in the specification at page 12, line 15 to page 22, line 11.

- Also, in formula 1 at page 13, the specification discloses examples of genes in transformants used for production of uridine diphospho-glucose (UDP-Glc) and biosynthetic pathway of UDP-Glc. In formula, (3) glucose-1-phosphate uridyltransferase (EC.2.7.7.9) has a known activity to produce UDP-Glc from glucose-1-phosphate (G-1-P) and UTP.

In Example 2 at specification page 67, line 20 to page 70, line 11, UDP-Glc is produced by using, enzyme sources, cells of *Corynebacterium ammoniagenes* and cells of recombinant *Escherichia coli* having DNA (galU gene) encoding glucose-1-phosphate uridyltransferase.

Accordingly, it is readily understood that UTP is produced from a nucleotide precursor and G-1-P derived from a sugar and UTP are converted to UDP-Glc.

2/ Or a treated product of the culture broth.

3/ Although the term does not appear in haec verba such is not required. All Dental Prod X LLC v. Advantage Dental Products Inc., 64 USPQ2d 1945 (Fed. Cir. 2002).

Moreover, the specification preferably omits what is well-known to those of ordinary skill. Spectra-Physics, Inc. v. Coherent, Inc., F.2d 1524 (Fed. Cir 1987).

- Specification page 14, formula 2 discloses examples of genes in transformants used for production of uridine diphospho-galactose (UDP-Gal) and biosynthetic pathway of UDP-Gal. In formula 2, (6) galactose-1-phosphate uridyltransferase (EC 2.7.7.12) produces UDP-Gal from galactose-1-phosphate (Gal-1-P) and UTP.

At Example 4 (page 72, line 18 to page 74, line 2), the specification discloses that UDP-Gal can be produced by using, as enzyme sources, cells of *Corynebacterium ammoniagenes* and of recombinant *Escherichia coli* having DNA (GalT gene) encoding galactose-1-phosphate uridyltransferase.

Based on formula 2 and Example 4, UTP is produced from a nucleotide precursor and Gal-1-P derived from a sugar and UTP are converted to UDP-Glc.

- Formula 3, at specification page 17 discloses examples of genes in transformants used for production of uridine diphospho-N-acetylglucosamine (UDP-GlcNAc) and biosynthetic pathway of UDP-Gal including (10) N-acetylglucosamine-1-phosphate uridyltransferase (EC 2.7.7.23), which produces UDP-GlcNAc from N-acetylglucosamine-1-phosphate (GlcNAc-1-P) and UTP.

Example 9 (at page 87, line 12 to page 88, line 12), discloses that UDP-GlcNAc can be produced using cells of *Corynebacterium ammoniagenes* and recombinant *Escherichia coli* having DNA (glmU gene) encoding N-acetylglucosamine-1-phosphate uridyltransferase.

Thus, based on the formula 3 and Example 4, UTP is produced from a nucleotide precursor, and GlcNAc-1-P derived from a sugar and UTP are converted to UDP-GlcNAc by glumU.

- At page 20, formula 6, discloses examples of genes in transformants used for production of uridine diphospho-mannose (GDP-Man) and biosynthetic pathway of GDP-Man. In formula 6, (18) mannose-1-phosphate guanyltransferase (EC 2.7.7.13) produces GDP-Man from mannose-1-phosphate (Man-1-P) and GTP.

In Example 14 at page 95, line 15 through page 96, the specification discloses that GDP-Man can be produced by using *Corynebacterium ammoniagenes* and *Escherichia coli* having DNA (manC gene) encoding mannose-1-phosphate uridyltransferase.

Accordingly, based on formula 6 and Example 14, GTP is produced from a nucleotide precursor and Man-1-P derived from a sugar and GTP are converted to GDP-Man by manC.

- At page 21 to page 22, line 1, the specification discloses examples of genes in transformants used for production of uridine diphospho-fucose (GDP-Fuc) and biosynthetic pathway of GDP-Fuc. In formula 6, (18) mannose-1-phosphate guanyltransferase (EC 2.7.7.13) produces GDP-Man from mannose-1-phosphate (Man-1-P) and GTP, and GDP-Man is converted into GDP-Fuc according to the reaction shown in formula 7.

Example 16 (page 98, line 8 to page 99, line 9) discloses that GDP-Man can be produced by using, *Corynebacterium ammoniagenes* and recombinant *Escherichia coli* having DNA (manC gene) encoding mannose-1-phosphate uridyltransferase.

Based on these descriptions, GTP is produced from a nucleotide precursor and Man-1-P derived from a sugar and GTP are converted to GDP-Man by manC to thereby produce GDP-Fuc.

Accordindingly, withdrawal of the rejection is respectfully requested.

Claims 1, 5, 15, 16, 18-20 and 72 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Akihiko et al., (EP 0 553 821 A1, dated 4-8-93)., Zapata et al. (J. Biol. Chem., Vol. 264(25):14769-14774) and knowledge that CMP-NeuAc can be synthesized from CTP and NeuAc (Stryer Biochemistry, 3rd Ed, 1988). This rejection is respectfully traversed as well.

In support of the Office Action, the Examiner asserts that since Akihiko teach microorganisms that produce UTP from orotic acid, and Zapata teaches a clone that can form CMP-sialic acid from sialic acid and CTP, one of ordinary skill in the art would produce GDP-sugar an appropriate synthetase enzyme.

As recited on claim 1, the present invention relates to a process for producing GDP-sugar or UDP-sugar using particular enzyme sources, a) capable of producing GTP or UTP from a nucleotide precursor, and b) from a microorganism having genes responsible for production of GDP-sugar or UDP-sugar from a sugar[4/] and GTP or UTP.

As pointed out by the Examiner, sialic acid synthase is an enzyme which forms CMP-sialic acid from CTP and sialic acid. That is, it is an enzyme which directly converts sialic acid into the sugar nucleotide CMP-sialic acid.

On the other hand, the synthase of GDP-sugar or UDP-sugar is an enzyme which forms GDP-sugar or UDP-sugar from GTP or UTP and sugar-1-phosphate as shown in formula 1 on page 13, formula 2 on page 14, formula 3 on page 17 and formula 6 on page 20 in the specification.

4/ Selected from the group consisting of glucose, fructose, galactose, glucosamine, N-acetylglucosamine, N-acetylgalactosamine, mannose, fucose and N-acetylmannosamine.

That is, claim 1 relates to a process for producing GDP-sugar or UDP-sugar without using a direct substrate of a sugar nucleotide synthase, i.e., without (an expensive) sugar-1-phosphate, but using instead a simple sugar such as glucose, etc., which is not a direct substrate of a sugar nucleotide synthase.

Accordingly, even combining Akihiko and Zapata only a process for producing UDP-sugar using a sugar nucleotide synthase with sugar-1-phosphate as a direct substrate of the sugar nucleotide synthase would result. However, no process using a simple sugar would be attained. Accordingly, there is no *prima facie* obviousness over the prior art.

In view of the above amendment and remarks, Applicants submit that all of the Examiner's concerns are now overcome and the claims are now in allowable condition. Accordingly, reconsideration and allowance of this application is earnestly solicited.

Claims 1, 5, 15, 16, 18-20 and 72 remain presented for continued prosecution.

Applicants' undersigned attorney may be reached in our New York office by telephone at (212) 218-2100. All correspondence should continue to be directed to our below listed address.

Respectfully submitted,

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Revised Notice*

AMENDMENTS MAY NOW BE SUBMITTED IN REVISED FORMAT

The United States Patent and Trademark Office (USPTO) is permitting applicants to submit amendments in a revised format as set forth below. Further details of this practice are described in *AMENDMENTS IN A REVISED FORMAT NOW PERMITTED*, signed January 31, 2003, expected to be published in *Official Gazette* on February 25, 2003 (Notice posted on the Office's web site at http://www.uspto.gov/web/offices/pac/dapp/opla/preognotice/revamdtprac.htm). The revised amendment format is essentially the same as the amendment format that the Office is considering adopting via a revision to 37 CFR 1.121 (Manner of Making Amendments). The revision to 37 CFR 1.121 (if adopted) will simplify amendment submission and improve file management. The Office plans to adopt such a revision to 37 CFR 1.121 by July of 2003, at which point compliance with revised 37 CFR 1.121 will be mandatory.

Effective immediately, **all** applicants may submit amendments in reply to Office actions using the following format. Participants in the Office's electronic file wrapper prototype[1] receiving earlier notices of the revised practice may also employ the procedures set out below.

REVISED FORMAT OF AMENDMENTS

Begin on separate sheets:
Each section of an Amendment (e.g., Claim Amendments, Specification Amendments, Drawing Amendments, and Remarks) should begin on a separate sheet. *For example*, in an amendment containing a.) introductory comments, b.) amendments to the claims, c.) amendments to the specification, and d.) remarks, each of these sections must begin on a separate sheet. This will facilitate the process of separately indexing and scanning of each part of an amendment document for placement in an electronic file wrapper.

Two versions of amended part(s) no longer required:
The current requirement in 37 CFR 1.121(b) and (c) to provide two versions (a clean version and a marked up version) of each replacement paragraph, section or claim will be waived where an amendment is submitted in revised format below. The requirements for substitute specifications under 37 CFR 1.125 will be retained.

A) **Amendments to the claims:**
Each amendment document that includes a change to an existing claim, or submission of a new claim, **must include a complete listing** of all claims in the application. After each claim number, the status must be indicated in a parenthetical expression, and the text of each claim under examination (with markings to show current changes) must be presented. The listing will serve to replace all prior versions of the claims in the application.

(1) The current status of all of the claims in the application, including any previously canceled or withdrawn claims, must be given. Status is indicated in a parenthetical expression following the claim number by one of the following: (original), (currently amended), (previously amended), (canceled), (withdrawn), (new), (previously added), (reinstated – formerly claim #_), (previously reinstated), (re-presented – formerly dependent claim #_), or (previously re-presented). The text of all pending claims under examination must be submitted each time any claim is amended. Canceled and withdrawn claims should be indicated by only the claim number and status.

(2) All claims being currently amended must be presented with markings to indicate the changes that have been made relative to the immediate prior version. The changes in any amended claim should be shown by strikethrough (for deleted matter) or underlining (for added matter). An accompanying clean version is not required and should not be presented. Only claims of the status "currently amended" will include markings.

(3) The text of pending claims not being amended must be presented in clean version, i.e., without any markings. Any claim text presented in clean version will constitute an assertion that it has not been changed relative to the immediate prior version.

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[1] The Office's Electronic File Wrapper prototype program is described in *USPTO ANNOUNCES PROTOTYPE OF IMAGE PROCESSING*, 1265 *Off. Gaz. Pat. Office* 87 (Dec. 17, 2002) ("Prototype Announcement"), and applies only to Art Units 1634, 2827 and 2834.

(4) A claim may be canceled by merely providing an instruction to cancel. Listing a claim as canceled will constitute an instruction to cancel. Any claims added by amendment must be indicated as (new) and shall not be underlined.

(5) All of the claims in each amendment paper must be presented in ascending numerical order. Consecutive canceled or withdrawn claims may be aggregated into one statement (e.g., Claims 1 – 5 (canceled)).

Example of listing of claims (use of the word "claim" before the claim number is optional):

Claims 1-5 (canceled)

Claim 6 (withdrawn)

Claim 7 (previously amended): A bucket with a handle.

Claim 8 (currently amended): A bucket with a ~~green~~ blue handle.

Claim 9 (withdrawn)

Claim 10 (original): The bucket of claim 8 with a wooden handle.

Claim 11 (canceled)

Claim 12 (re-presented – formerly dependent claim 11) A black bucket with a wooden handle.

Claim 13 (previously added): A bucket having a circumferential upper lip.

Claim 14 (new): A bucket with plastic sides and bottom.

B) Amendments to the specification:

Amendments to the specification must be made by presenting a replacement paragraph or section marked up to show changes made relative to the immediate prior version. An accompanying clean version is not required and should not be presented. If a substitute specification is being submitted to incorporate extensive amendments, both a clean version (which will be entered) and a marked up version must be submitted as per current 37 CFR 1.125.

C) Amendments to drawing figures:

Drawing changes must be made by presenting replacement figures which incorporate the desired changes and which comply with § 1.84. An explanation of the changes made must be presented in the remarks section of the amendment. Any replacement drawing sheet must include all of the figures appearing on the immediate prior version of the sheet, even though only one figure may be amended. The figure or figure number of the amended drawing should not be labeled as "amended." If the changes to the drawing figure(s) are not accepted by the examiner, applicant will be notified of any required corrective action in the next Office action. No further drawing submission will be required, unless applicant is notified.

Any questions regarding the submission of amendments pursuant to the revised practice set forth in this flyer should be directed to the following legal advisors in the Office of Patent Legal Administration (OPLA): Elizabeth Dougherty (Elizabeth.Dougherty@uspto.gov), Gena Jones (Eugenia.Jones@uspto.gov) or Joe Narcavage (Joseph.Narcavage@uspto.gov). For information on the waiver or legal aspects of the prototype, please contact Jay Lucas (Jay.Lucas@uspto.gov), Senior Legal Advisor (PCTLA) or Rob Clarke (Robert.Clarke@uspto.gov), Senior Legal Advisor (OPLA). Alternatively, further information may be obtained by calling OPLA at (703) 305-1616.

* Revised Notice: See Sec. B) for changes relating to substitute specifications, and Sec C) for changes on replacement drawing practice.